

Fig. 4

Fig. 5

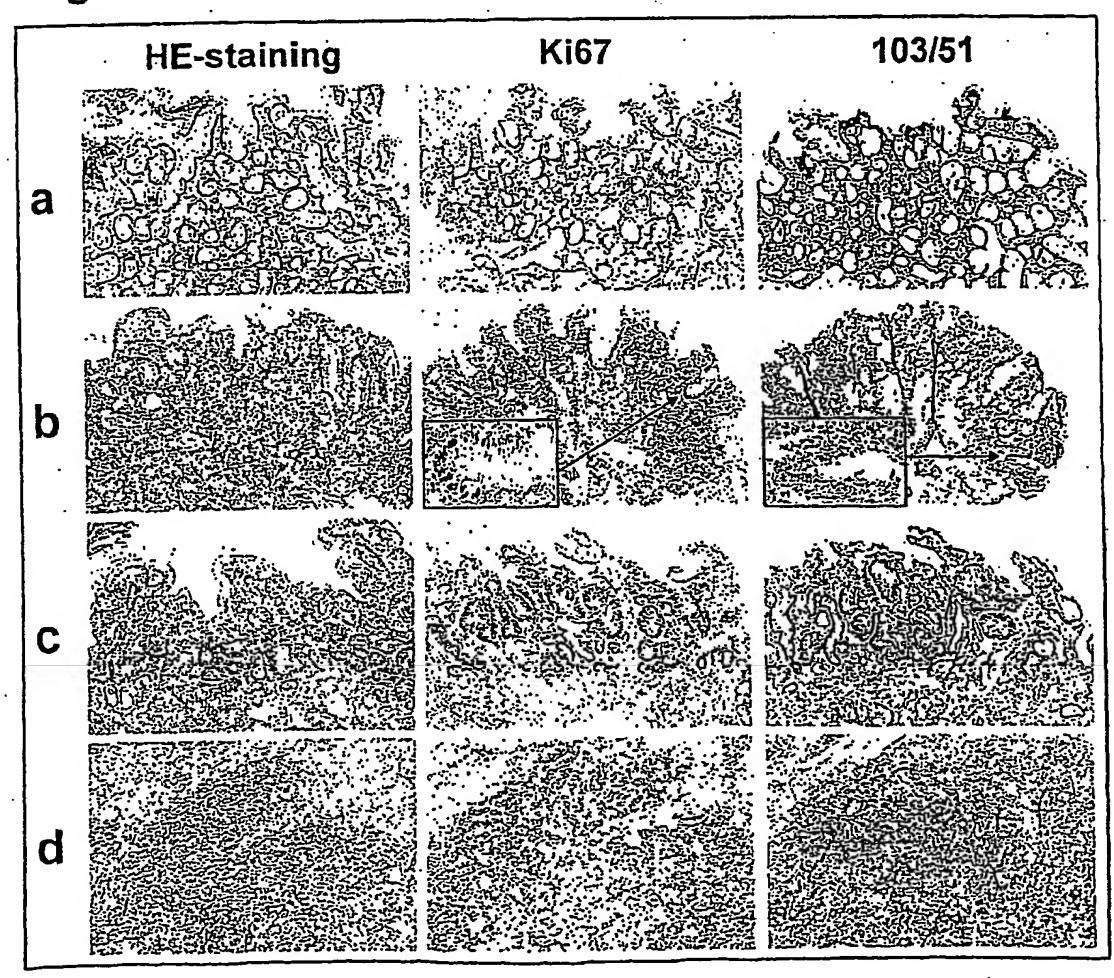


Fig. 6

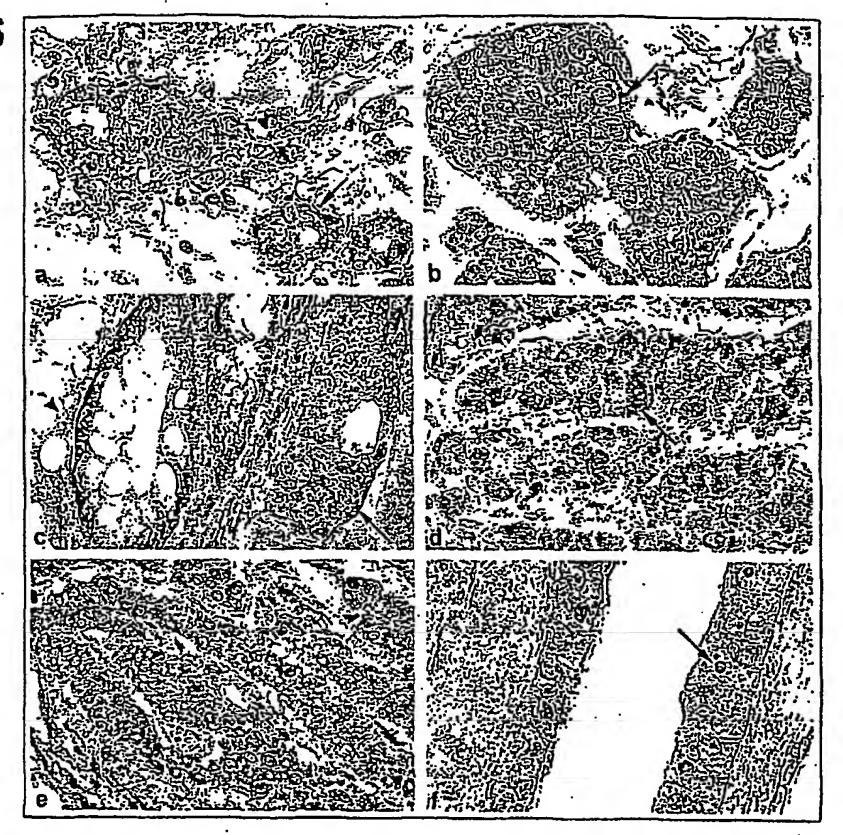
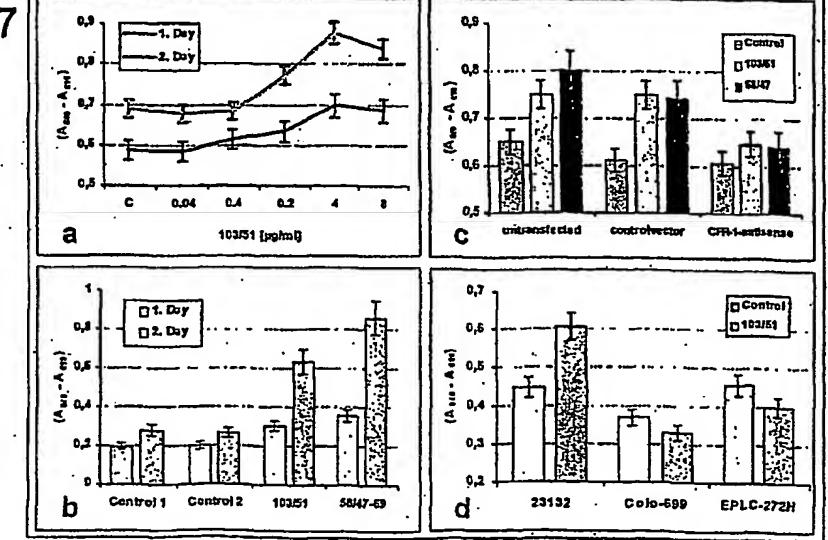


Fig. 7



tcc Ser 1	tgc Cys	aag Lys	gct Ala	tct Ser 5	ġgc Gly	tac Tyr	acc	ttc Phe	act Thr 10	gac	tac Tyr	tat Tyr	ata Ile	aac Asn 15	45
tgg Trp	gtg Val	aag Lys	cag Gln	agg Arg 20	act Thr	gga Gly	cag	GJÀ 88c	ctt Leu 25	gag Glu	tgg Trp	att Ile	gga Gly	gag Glu 30	90
att Ile	tat Tyr	cct Pro	gga Gly	agt Ser 35	ggt Gly	aat Asn	act Thr	tac Tyr	tac Tyx 40	aat Asn	Gl <i>i</i> i gag	aag Lys	ttc Phe	aag Lys 45	135
Gly	aag Lys	gcc Ala	aca Thr.	ctg Leu 50	act Thr	gca Ala	gac Asp	aaa Lys	tcc Ser 55	tcc Ser	agc Ser	aca Thr	gcc Ala	tac Tyr 60	180
atg Met	Gln	ctc Leu	agc Ser	agc Ser 65	ctg Leu	aca Thr	tct Ser	gag Glu	gac Asp 70	tct Ser	gca Ala	gtc VaI	tat Tyr	Phe 75	225
tgt Cys	gca Ala	aga Arg	tcg Ser	gga Gly 80	tta [.] Leu	cga Arg	ecc Pro	tat Tyr	gct Ala 85	atg Met	gac Asp	tac Tyr	tgg Trp	ggt Gly 90	270
		acc Thr													

Fig. 8A

Fig. 8B

Nucleotide sequence of the variable region of the heavy chaln (VH) of antibody NM58-49/69

		0 6		135	180		225		270		95
	aac Asn 15	9ag Glu 30		aag Lys 45	tac Tyr 60		ttc Phe 75		ggt Gly 90		
	ata Ile	G1у		ttc Phe	gcc Ala		tat Tyr		tgg Trp		
CDR1	tat Tyr	II the tr		aag Lys	aca Thr		gtc Val		tac Tyr		
ਹ	tac Tyr	tgg Trp		gag Glu	agc Ser		.gca Ala	ene	gac Asp		
	дас Авр	gag G1u		aat Asn	Ser	٠.	tot. Ser	J-gene	atg Met		
		ott Leu 25		tac Tyr 40	tcc Ser .55	• •	gac Asp 70	l	gct Ala 85		
	ttc act Phe:Thr 10	99c Gly	CDR2	tac Tyr	aaa Lys		gag Glu		tat Tyr		
	acc Thr	cag Gln		act Thr	gас Авр	•	rct Ser	CDR3	ccc Pro		
	tac Tyr	9ga G1y	Į	aat Aen	gca Ala	•	aca Thr		cga Arg		
	99c 61y	act Thr		ggt Gly	act Thr		ctg	on l	tta Leu		acc
	tct Ser s	agg Arg 20		agt Ser 35	ctg Leu 50		agc.ctg Ser Leu 65	D-gene	9ga G1y 80		gtc Val
	gct Ala	cag Gln	ļ	gga Gly	aca Thr		agc Ser		tag Ser	•	tcai
	aag Lys	аад Lys		cct Pro	gcc Ala		oto Leu		aga Arg		acc Thr
	tgc Cys	gtg Val		tat Tyr	aag Lys		cag Gln		gca Ala		gga Gly
	Ser 1	tgg Trd		att Ile	ggc		atg Met	•	tgt Cys		Gln
		•					•				

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cca Pro 1	ctc Leu	tcc Ser	ctg Leu	cct Pro 5	gtc Val	agt Ser	ctt Leu	gga Gly	gat Asp 10	caa Gln	gcc Ala	tec Ser	atc Ile	tct Ser 15	45
tgc Cys	aga Arg	tct Ser	agt Ser	Cag Gln 20	agc Ser	att Ile	gta Val	cat His	agt Ser 25	Asn	gga Gly	aac Asn	acc Thr	tat Tyr 30	90
tta Leu	gaa Glu	tgg Trp	tac Tyr	ctg Leu 35	cag Gln	aaa Lys	bró cca	ggc Gly	cag Gln 40	tct Ser	cca Pro	rys 88g	ctc Leu	ctg Leu 45	135
atc Ile	tac Tyr	Lys	gtt Val	tcc Ser 50	aac ,Asn	Arg	ttt Phe	tct Ser	999 955	gtc Val	cca Pro	gac	agg Arg	ttc Phe 60	180
agt Ser	ggc	agt Ser	Gly	tca Ser 65	G1y 999	aca Thr	gat Asp	ttc Phe	aca Thir 70	ctc Leu	aag Lys	atc Ile	agc	aga Arg 75	. 225
gtg Val	Glu gag	gct Ala	gag Glu	gat Asp 80	ctg Leu	GJ y gga	gtt Val	tat Tyr	tac Tyr 85	tgc Cys	ttt Phe	ćaa Gln	ggt Gly	tca Ser 90	270
cat His	gtt Val	ccg Pro	tac Tyr	acg Thr 95	ttc Phe	Gly	999 999	Gly 999	acc Thr 100	.aag Lys	ctg Leu	gaa Glu	ata Ile	aaa Lys 105	315.

Fig. 9A

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Fig. 9B

Nucleotide sequence of the variable region of the light chain (VL) of antibody NM58-49/69

<u>ል</u> ረ		06 .	135		180	225		270		315
ser 15		Tyr 30	ctg Leu 45		ttc Phe 60	aga Arg 75	33	tca Ser 90		aaa Lya 105
atc Ile		Thr	ctc Leu		agg Arg	agc Ser	CDR3	ggt Gly		ata Ile
Ser	:	aac Asn	aag Lys		gac Ago	atc .Ile		caa Gln		gaa Glu
gcc Ala	:	gga	cca Pro		GCCa Pro	аад Lyв		ttt		ctg Leu
caa Gln		aat Asn	tct Ser		gtc Val	cto Leu		tgc Cya		аад Lув
gga gat Gly Asp 10	CDR1	agt Ser 25	cag Gln 40		999 617 55	aca Thr 70		tac Tyr 85	•	acc Thr 100
99a 61y	Ö	cat His	ggc Gly		ser	ttc Phe		tat Tyr		999 G1y
ctt Leu	i	gta Val	cca Pro		ttt	gat Asp		gtt Val [.]		999 61y
agt	•	att Ile	ааа Lys		cga Arg	aca Thr		gga Gly		gga Gly
gtc Val		agc Ser	cag Gln	CDR2	aac Asn	999 G1y		ctg Leu		ttc Phie
cca ctc tcc ctg cct gtc agt Pro Leu Ser Leu Pro Val Ser 1	!	cag Gln 20	ctg Leu 35		tcc Ser 50	tca Ser 65		gat Asp 80	ţ	acg Thr 95
ctg Leu		agt Ser	tac Tyr		gtt Val	agt gga Ser Gly		gag Glu		tac Tyr
Ser	!	tot Ser	tgg Trp		ааа Lyв	agt Ser		gct		acg Pro
ctc Leu		aga Arg	gaa Glü		Tyr	ggc Gly		gag Glu		gtt Val
cca Pro 1		tgc Cys	tta Leu		atc Ile	agt. Ser		gtg Val		cat His

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gat Asp	gtg Val	agg Arg	gag Glu	Pro 5	gaa Glu	aat Asn	gaa Glu	att Ile	tct Ser 10	tca Ser	gac Asp	tgc Cys	aat Asn	cat His 15		45
ttg Leu	ttg Leu	tgg Trp	aat Asn	tat Tyr 20	aag Lys	ctg Leu	aac Asn	cta Leu	act Thr 25	aca Thr	gat Asp	ccc Pro	aaa Lys	ttt Phe 30		90
gaa Glu	tct Ser	Val 9tg	gcc Ala	aga Arg 35	gag Glu	gtt Val	tgc Cys	aaa Lys	tct Ser 40	act Thr	ata Ile	aca Thr	gag Glu	att Ile 45		135
gaa Glu	gaa Glu	tgt Cys	gct	gat Asp 50	gaa Glu	ccg Pro	gtt Val.	gga Gly	aaa Lys 55	ggt Gly	tac Tyr	atg Met	gtt Val	tcc Ser 60		180
tgc Cys	ttg Leu	gtg Val	gat Asp	Cac His 65	cga Arg	ggc ggc	aac Asn	atc Ile	act Thr 70	gag Glu	tat Tyr	cag Gln	tgt Cys	cac His 75		225
GJu. caā	tac Tyr	att Ile	Thr	aag Lys 80	atg Met	acg Thr	gcc Ala	atc Ile	att Ile 85	ttt Phe	agt Ser	gat Asp	tac Tyr	cgt Arg 90	,	270
tta Leu	atc Ile	tgt Cys	Gly	ttc Phe 95	atg Met	gat Asp	ġac Așp	tgc Cys	aaa Lys 100	aat Asn	gac Asp	atc Ile	aac Asn	att Ile 105		315
ctg Leu	aaa Lys	tgt Cys	ggc	agt Ser 110	att Ile	cgg	ctt Leu	gga Gly	gaa Glu 115	aag Lys	gat Asp	gca Ala	cat His	tca Ser 120	·	360
caa Gln	ggt Gly	gag Glu	gtg Val	gta Væl 125	tca Ser	tgc Cys	ttg Leu	gag Glu	Tys 130	ggc	ctg Leu	gtg Val	aaa Lys :	gaa Glu 135	•	405
					Pro											450
Lys	Ala	Ile	Leu	Arg 155	gtg Val	Ala	Glu	Leu	Ser 160	Ser	Asp	Asp	Phe	His 165		495
Leu	yap	Arg	His	Leu 170	tat Tyr	Phe	Ala	Сув	Arg 175	Asp	Asp	Arg	Glu	Arg 180		540
-Phe	Cys	Glu	Asn	Thr 185	caa Gln	Ala	,Gly	Glu	Gly 190	Arg	Val	Тух	Lys	Cys 195		585
ctc Leu	Phe	Asn;	cat His	aaa Lys 200	Phe	gaa Glu	gaa Glu	tcc Ser	atg Met 205	agt Ser	gaa Glu	. Lys	tgt Cys	cga Arg 210		630

Fig. 10-1

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gaa Glu	·gca Ala	ctt Leu	aca	acc Thr 215	cgc Arg	caa Gln	aag Lys	ctg Leu	att Ile 220	gcc Ala	cag Gln	gat Asp	tat	aaa Lys 225		·675
gtc Val	agt Ser	tat Tyr	tca Ser	ttg Leu 230	gcc Ala	. aaa Lys	tcc Ser	tgt Cys	aaa Lys 235	agt Ser	gac Asp	ttg Leu	aag Lys	aaa Lys 240		720
			aat Asn													765
ctc Leu	tcc Ser	tac	ttg Leu	tta Leu 260	atġ Met	tgc Cys	ctg Leu	gag Glu	tca Ser 265	gct Ala	gta .Val	cac His	aga Arg	999 Gly 270		810
			agc Ser													85S
			atg Met		Asp	_										900
			Gly 999													945
			acc													990
Lys	Gly	Asn	ctt Leu	Gly 335	Met	Asn	Cys	Gln	Gln 340	Ala	Leu	Gln	Thr	Leu 345		1035
Ile	Gln	Glu	act	Asp 350	Pro	Gly	Ala	Asp	Tyr 355	Arg	Ile	Asp	Arg	Ala		1080
Leu	Asn	Glu	gct Ala	Cys 365	Glu	Ser	Val	Ile	Gln 370	Thr	Ala	Сув	Lys	His 375	•	1125
Ile	Arg	Ser	gga	Asp 380	Pro	Met	Ile	Leu	Ser 385	Cys	Leu	Met	Ġļu	His 390		1170
Leu	Tyr	Thr		Lу в 395	Met	Val	Glu	Asp	Cys 400	Glu	His	Arg	Leu	Leu 405		1215
Glu	Leu	Gln	Tyr	Phe 410	Ile	Ser	Arg	Asp	Trp 415	Lys	Len	Asp	Pro	420		. 1260
														acc Thr 435		1305
	_	-	aat Asn	_	_				_			_	_	gtg Val 450		1350
			Leu											gga Gly 465		1395

Fig. 10-2

			tca Ser		_						-					1440
	_	_	gcc	_	_			_	_		_			_		1485
			att			_					_		_	-		1530
	_	_	Lys	-					_		_	_	_			1575
_			tgt Cys				-					_				1620
			att Ile							_		_	_	_ , _		1665
			Gln Gln		Phe		_			Ala	Asp		Gln			1710
			gac Asp													1755
			asc										Phe			1800
Leu	Val	Gln	atg Met	Lys 605	Asp	Phe	Arg	Phe	Ser 610	Tyr	Lys	Phe	Lys	Met 615	٠	.1845
Ala	Сув	. Lys	Glu gag	Asp 620	Val	Leu	Lys	Ļeu	Сув 625	Pro	Asn	Ile	Гув	630		1890
Lys	Val	Asp	Val	Val 635	Ile	Cys	Ļeu	Ser	Thr 640	Thr	Val	Arg	Asn	gac Asp 645		1935
	Leu	Gln	Glu	Ala 650	Lys	Glu	His	Arg	Val 655	Ser	Leu	Lys	Сув	Arg 660		1980
			Arg							Thr				cgc Arg 675		2025
										Ser				aac Asn 690	·	2070
										Gln				tgt Cys 705		2115
_		_						_		Arg	_			aaa Lys 720		2160

Fig. 10-3

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gta Val	ttt Phe	rys Fas	ctg Leu	cag Gln 725	gag Glu	aca Thr	gag Glu	atg Met	atg Met 730	gac Asp	cca Pro	gag Glu	cta Leu	gac Asp 735		2205
tac	acc	ctc Leu	atg. Met	agg Arg 740	gtc Val	tgc Cys	aag Lys	cag	atg Met 745	ata Ile	Lys Lys	aag Lys	Phe	tgt Cys 750		2250
ccg Pro	gaa Glu	gca Àla	Asp	tct Ser .755	aaa Lys	acc	atg Met	ttg Leu	cag Gln 760	tgc Cys	ttg Leu	aag Lys	caa Gln	aat Asn 765	•	2295
aaa Lys	aac Asn	agt Ser	gaa Glu	ttg Leu 770	atg Met	gat Asp	ccc Pro	aaa Lys	tgc Cys 775	aaa Lys	cag Gln	atg Met	ata Ile	acc Thr 780		2340
aag Lys	cgc	cag Gln	atc Ile	acc Thr 785	Gln	aac Asn	aca Thr	gat Asp	tac Tyr 790	cgc Arg	tta Leu	aac Asn	Pro	atg Met 795		2385
tta Leu	aga Arg	aaa Lys	gcc Ala	tgt Cys 800	aaa Lys	gct	gac Asp	att Ile	cct Pro 805	aaa Lys	ttc Phe	tgt Cys	cac His	ggt Gly 810		2430
atc	ctg Leu	act Thr	rys	gcc Ala 815	rys	gat Asp	gat	tca Ser	gaa Glu 820	tta Leu	gaa Glu	gga Gly	caa Gln	gtc Val 825	. • .	2475
									Sac Asp 835						·	2520
gac	tgt Cys	gaa Glu	Asp	Gln 845	atc Ile	cga Arg	atc Ile	att Ile	atc Ile 850	cag Gln	gag Glu	tcc Ser	Ala GCC	ctg Leu 855		2565
									ctg Leu 865						•	2610
									gca Ala 880						•	2655
									aac Asn 895					aaa Lys, 900		2700
									aac Asn 910							2745 ·
aaa Lys	gca Ala	9ac Asp	atc Ile	ttt Phe 920	gtt Val	gac Asp	ccg Pro	gta Val	ctt Leu 925	cat His	act Thr	gct Ala	tgt Cys	gcc Ala 930		2790
ctg Leu	gac	att Ile	Lys	cac His 935	cac His·	tgc Cys	gca Ala	gcc Ala	atc Ile 940	acc Thr	ect Pro	Gj A	cgc Arg	999 Gly 945		2835
cgt Arg	caa Gln	atg Met	Ser	tgt Cys 950	ctc Leu	atg Met	gaa Glu	gca	ctg Leu 955	gag Glu	gat Asp	aag Lys	cgg Arg	gtg Val 960	•	2880
			Pro ·						ct <i>c</i> Leu 970							2925

Fig. 10-4

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Met	Trp	Ser	Tyr	gca Ala 980	gca Ala	Lys	gtg Val	gcc	Pro 985	gca Ala	gat Asp	ggc ggc	ttc Phe	tct Ser 990		2970
gat' Asp	ctt Leu	gcc Ala	atg Met	caa Gln 995	gta Val	atg Met	acg Thr	tct Ser	cca Pro 1000	Ser	Lys	aac Asn	tac Tyr	att Ile 1005		3015
ctc Leu	tet Ser	gtg Val	atc Ile	agt Ser 1010	Gly	agc Ser	atc Ile	tgt Cys	ata Ile 1015	Leu	ttc Phe	ctg Leu	att Ile	ggc Gly 1020	•	3060
ctg Leu	atg Met	tgt Cys	ġġa Ģly	cgg Arg 1025	Ile	acc	aag Lys	cga Arg	gtg Val 1030	Thr	cga Arg	ejn ag	ctc Leu	aag LysA 1035		3105
_	agg		l										•			

Fig. 10-5

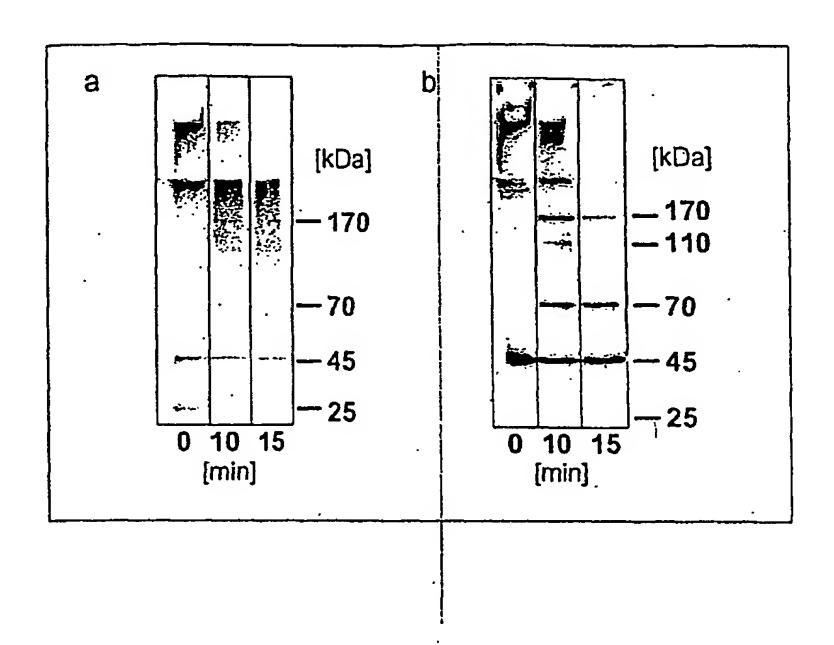
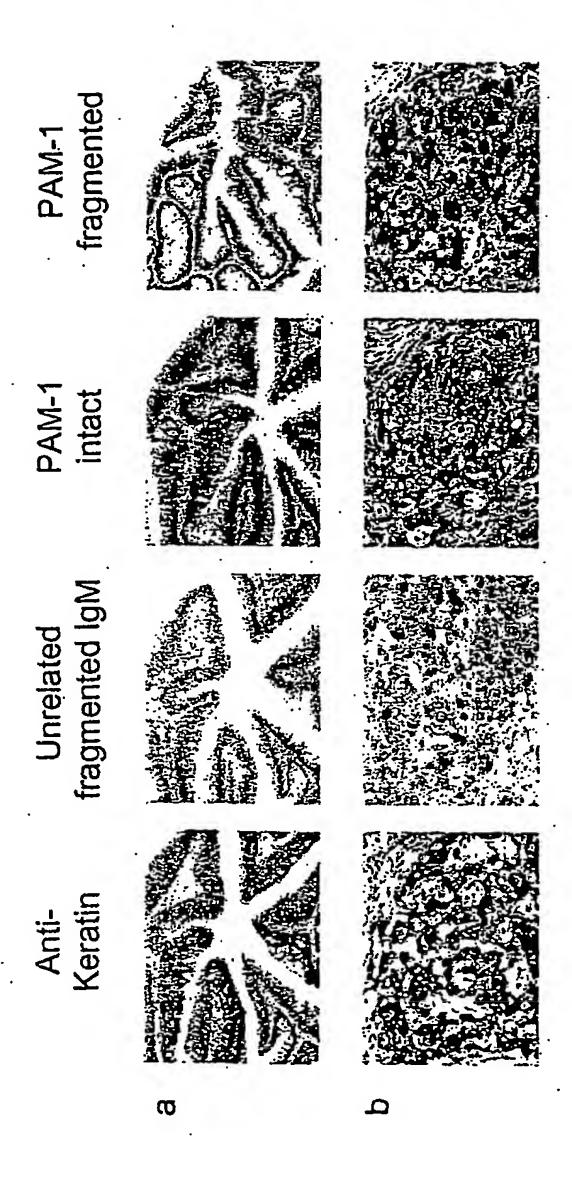
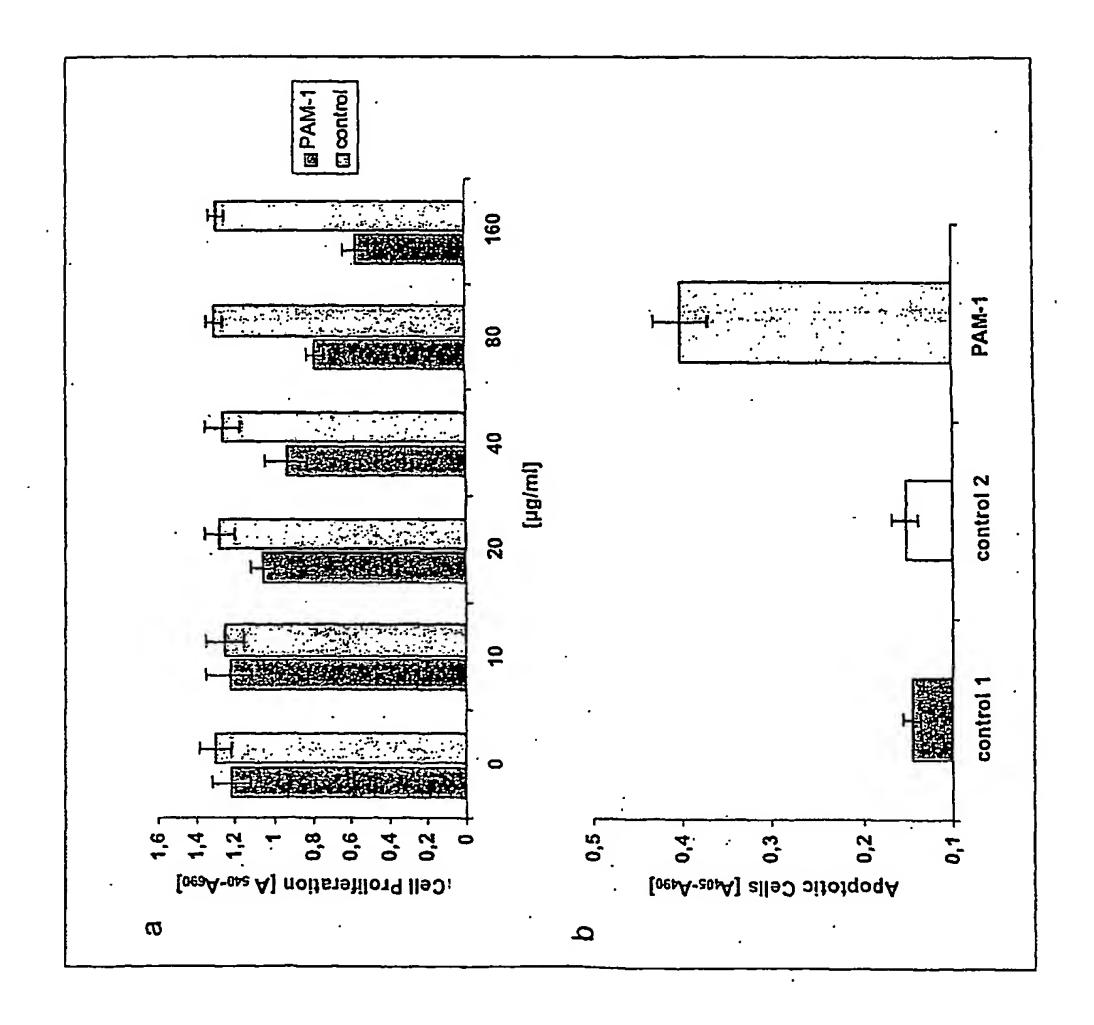


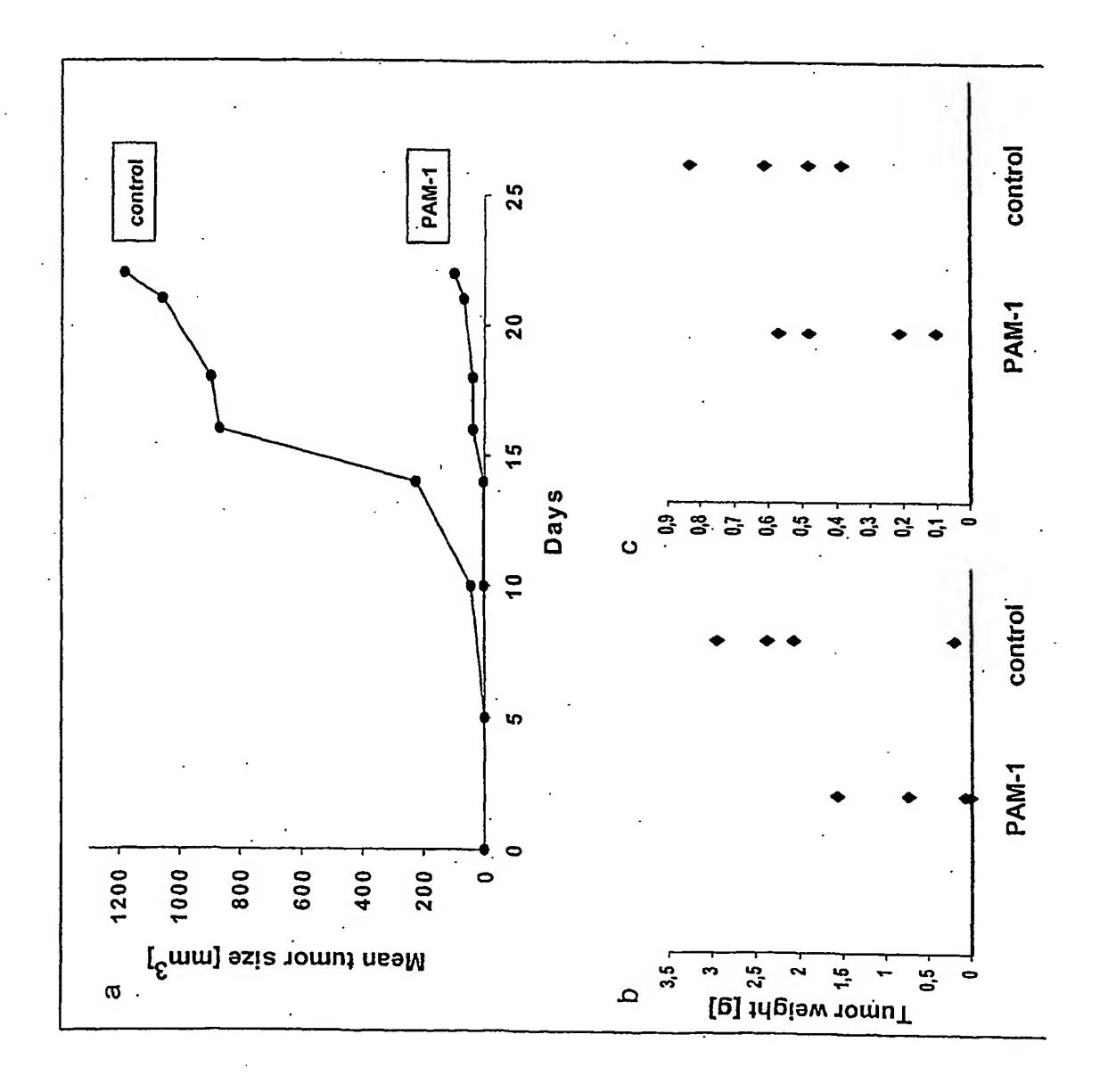
Fig. 11

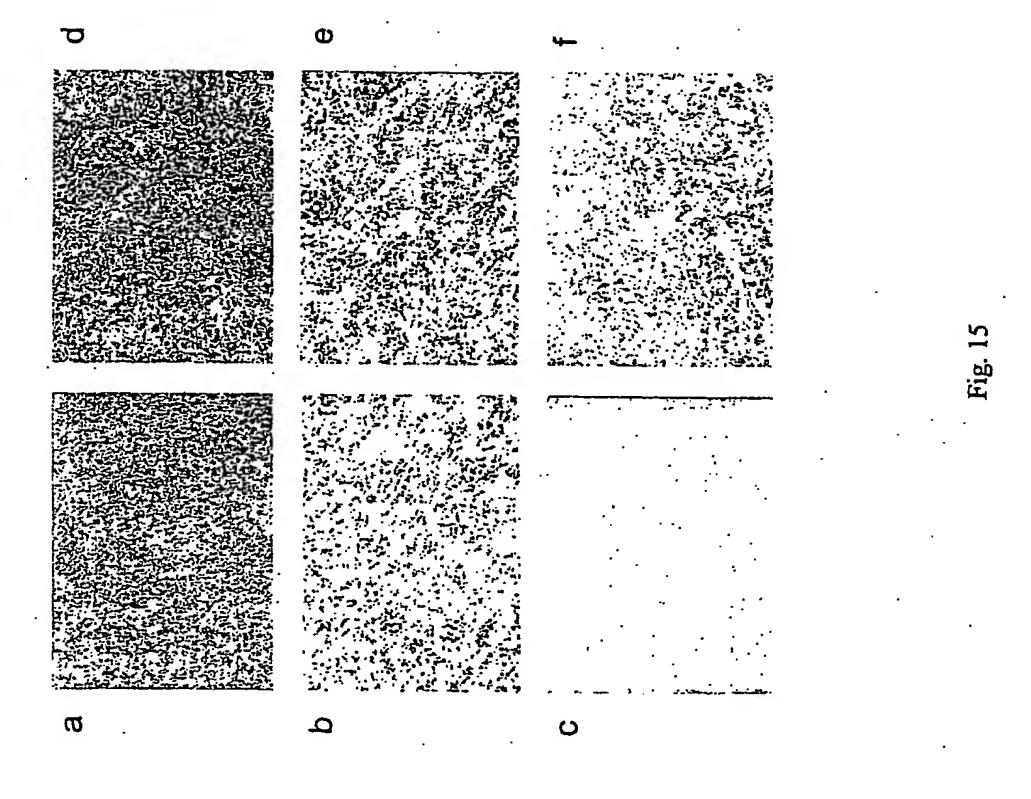


ig. 13



ig. 14





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RAINEACESV IQTACKHIRS GDPMISSCLM EHLYTEKAVE RAINEACESV IQTACKHIRS GDPMISSCLM EHLYTEKAVE YRTEEQGREL SAECRAEVQR ILHQRAMDVK LDPALQDKCL YRTEEQGREL SAECRAEVQR ILHQRAMDVK LDPALQDKCL YRTEEQGREL SAECRAEVQR ILHQRAMDVK LDPALQDKCL YRTEEQGREL SAECRAEVQR ILHQRAMDVK LDPALQDKCL ONFCHOVADN QIDSGDLMEC LIQNKHQKDM NEKCAIGVTH OPFCHO-ADN QIDSGDLMEC LIQNKHQKDM NEKCAIGVTH CRRQLRVEEL EMTEDIRLEP DLYEACKSDI KNFCSAVQYG CRRQLRVENNS ELMDPKCKQM ITKRQITQNT DYRLNPMLRK LQCLKQNKNS ELMDPKCKQM ITKRQITQNT DYRLNPMLRK LDPQLQLHCS DEISSLCAEE AAAQEQTGQV SECLKVNLLK	501 RALNEACESV IQTACKHIRS GDPMILSCLM EHLYTEKMVE 601 YRTEEQGRR: SRECRAEVQR ILHQRAMDVK LDPALQDKCL 601 YRTEEQGRR: SRECRAEVQR ILHQRAMDVK LDPALQDKCL 602 YRTEEQGRR: LDPALQDKCL IDLGKWCSEK TETGGELECL 701 QN7CHDVADN QIDSGDLMEC LIQNXHQKDM NEKCAIGVTH 701 QNFCHDVADN QIDSGDLMEC LIQNXHQKDM NEKCAIGVTH 701 QNFCHDVADN QIDSGDLMEC LIQNXHQKDM NEKCAIGVTH 801 CRRQLRVEEL EMTEDIRLEP DLYEACKSDI KNFCSAVQYG 801 CRRQLRVEEL EMTEDIRLEP DLYEACKSDI KNFCSAVQYG 801 LQCLKQNKNS ELMDPKCKQM ITKRQITQNT DYRLNPMLRK 901 LQCLKQNKNS ELMDPKCKQM SECLKVNLLK 1001 LDPQLQLHCS DEISSLCAEE AAAQEQTGQV SECLKVNLLK 1001 LDPQLQLHCS DEISSLCAEE AAAQEGTGQV SECLKVNLLK
RALNEACESV IQTACKHIRS GDPMILSCLM EHLYTEKAVE RALNEACESV IQTACKHIRS GDPMILSCLM EHLYTEKAVE RALNEACESV IQTACKHIRS GDPMILSCLM EHLYTEKAVE YRTEEQGRRI SRECRAEVQR ILHQRAMDVK LDPALQDKCL YRTEEQGRRI SRECRAEVQR ILHQRAMDVK LDPALQDKCL YRTEEGGRRI SAECRAEVQR ILHQRAMDVK LDPALQDKCL YRTEEGGRRI SAECRAEVQR ILHQRAMDVK LDPALQDKCL OFCHD-ADN QIDSGDLMEC LIQNKHQKDM NEKCAIGVTH QNFCHDVADN QIDSGDLMEC LIQNKHQKDM NEKCAIGVTH CRRQLRVEEL EMTEDIRLEP DLYEACKSDI KNFCSAVQYG LQCLKQNKNS ELMDPKCKQM ITKRQITQNT DYRLNPMLRK LQCLKQNKNS ELMDPKCKQM ITKRQITQNT DYRLNPMLRK LDPQLQLHCS DEISSLCAEE AAAQEQTGQV EECLKVNLLK LDPQLQLHCS DEISSLCAEE AAAQEQTGQV SECLKVNLLK LDPQLQLHCS DEISSLCAEE AAAQEQTGQV SECLKVNLLK RVALQPECKK RLNDRIEMWS YAAKVAPPADG FSDLAMQVMT RVALQPECKK RLNDRIEMWS YAAKVAPPADG FSDLAMQVWT RVALQPECKK RLNDRIEMWS YAAKVAPPADG FSDLAMQVWT RVALQPECKK RLNDRIEMWS YAAKVAPPADG FSDLAMQVWT	601 YRTEEGGRES SRECRAEVOR LIHORAMDVK LDPALQDKCL IDLGKWGSEK TETGGLECL QDHIJDLAVE 601 YRTEEGGRES SRECRAEVOR LIHORAMDVK LDPALQDKCL IDLGKWGSEK TETGGLECL QDHIJDLAVE 601 YRTEEGGRES SRECRAEVOR LIHORAMDVK LDPALQDKCL IDLGKWGSEK TETGGLECL QDHIJDLAVE 602 YRTEEGGRES LEAGENCEL ILHORAMDVK LDPALQDKCL IDLGKWGSEK TETGGLECL QDHIJDLAVE 603 YRTEEGGRES LEAGENCEL LIHORAMDVK LDPALQDKCL IDLGKWGSEK TETGGLECL QDHIJDLAVE 704 QTCCHDAVDN QIDSGDLWCC LIQNKHQKDM NEKCAIGVTH FQLVQMKDFR FSYKEFWACK EDVLKLCRNI 705 QTCCHDAVDN QIDSGDLWCC LIQNKHQKDM NEKCAIGVTH FQLVQMKDFR FSYKEFWACK EDVLKLCRNI 706 QTCCHDAVDN QIDSGDLWCC LIQNKHQKDM NEKCAIGVTH FQLVQMKDFR FSYKEFWACK EDVLKLCRNI 707 QTCCHDAVDN QIDSGDLWCC LIQNKHQKDM NEKCAIGVTH FQLVQMKDFR FSYKEFWACK EDVLKLCRNI 708 QTCCHDAVDN QIDSGDLWCC LIQNKHQKDM NEKCAIGTH FQLVQMKDFR FSYKEFWACK EDVLKLCRNI 709 QTCCHCONNUS ELMDENCKQM ITKRQITQNT DYRLNPMLRK ACKADIENEC HGILTFKAKDD SELSGGVISC 709 LQCLKQNNNS ELMDEKCKQM ITKRQITQNT DYRLNPMLRK ACKADIENEC HGILTFKAKDD SELSGGVISC 709 LQCLKQNNNS ELMDEKCKQM ITKRQITQNT DYRLNPMLRK ACKADIENEC HGILTFKAKDD SELSGGVISC 709 LQCLKQNNNS ELMDEKCKQM ITKRQITQNT DYRLNPMLRK ACKADIENEC HGILTFKAKDD SELSGGVISC 709 LDCLKQNNNS ELMDEKCKQM TTKRQITQNT DYRLNPMLRK ACKADIENEC HGILTFKAKDD SELSGGVISC 709 LDCLKQNNNS ELMDEKCK ALNDRIENWS YAAKVAPRADG FSDLAMQVWT SPSKNYILSV ISGSCTLEL IGLMCGRITFK 7101 RVALQPECKK ALNDRIENWS YAAKVAPRADG FSDLAMQVWT SPSKNYILSV ISGSCTLEL IGLMCGRITFK 7101 RVALQPECKK ALNDRIENWS YAAKVAPRADG FSDLAMQVWT SPSKNYILSV ISGSCTLEL IGLMCGRITFK 71101 RVALQPECKK ALNDRIENWS YAAKVAPRADG FSDLAMQVWT SPSKNYILSV ISGSCTLEL IGLMCGRITFK
RALNEACESV IGTACKHIRS GDPMIESCLM EHLYTEKNVE DCEHRLLELO YEISROWKLD RALNEACESV IGTACKHIRS GDPMIESCLM EHLYTEKNVE DCEHRLLELO YEISROWKLD RALNEACESV IGTACKHIRS GDPMILSCLM EHLYTEKNVE DCEHRLLELO YEISROWKLD YRTEEGGRRI. SRECRAEVOR ILHORAMDVK LDPALQDKCL IDLGKWCSEK TETGGELECL YRTEEGGRRI. SRECRAEVOR ILHORAMDVK LDPALQDKCL IDLGKWCSEK TETGGELECL YRTEEGGRRI. SRECRAEVOR ILHORAMDVK LDPALQDKCL IDLGKWCSEK TETGGELECL ONFORMADEN GIDSGDLMEC LIONKHOKOM NEKCAIGVTH FOLVOMKDER FSYKETWACK OTFCHOVADN GIDSGDLMEC LIONKHOKOM NEKCAIGVTH FOLVOMKDER FSYKETWACK GRECLAVZEL EMTEDIRLEP DLYEACKSDI KNFCSAVQYG NAQIIECLKE NKKQLSTRCH CRRQLRVEEL EMTEDIRLEP DLYEACKSDI KNFCSAVQYG NAQIIECLKE NKKQLSTRCH CLQCLKQNKNS ELMDPKCKOM ITKRQITQNT DYRLNPMLRK ACKADIPREC HGILTKAKDD LQCLKQNKNS ELMDPKCKOM ITKRQITQNT DYRLNPMLRK ACKADIPREC HGILTKAKDD LLQCLKQNKNS ELMDPKCKOM ITKRQITQNT DYRLNPMLRK ACKADIPREC HGILTKAKDD LDPQLQLHCS DEISSLCAEE AAAQEQTGQV EECLKVNLLK IKTELCKKEV LNMLKESKAD LDPQLQLHCS DEISSLCAEE AAAQEQTGQV EECLKVNLLK IKTELCKKEV LNMLKESKAD LDPQLQLHCS DEISSLCAEE AAAQEQTGQV EECLKVNLLK IKTELCKKEV LNMLKESKAD LDPQLQHCS DEISSLCAEE AAAQEQTGQV EECLKVNLLK IKTELCKKEV LNMLKESKAD LDPQLQHCS DEISSLCAEE AAAQEQTGQV EECLKVNLLK IKTELCKKEV LNMLKESKAD SURVALQPECKK RLNDRIEMWS YAAKVAPRADG FSDLAMQVMT SPSKNYILSV ISGSICILEL INVALQPECKK RLNDRIEMWS YAAKVAPRADG FSDLAMQVMT SPSKNYILSV ISGSICILEL INVALQPECKK RLNDRIEMWS YAAKVAPRADG FSDLAMQVMT SPSKNYILSV ISGSICILEL INTALCELLEL	501 RALNEAGESV IGTACKHIIS GDEMILSCLM EHLYTEKNVE DCEHRLLELO YFISAJWKLD 601 YRTEEGGRRI SRECRAEVOR ILHORAMDVK LDPALQDKCI IDLGKWGSEK TETGGELECL 601 YRTEEGGRRI SRECRAEVOR ILHORAMDVK LDPALQDKCI IDLGKWGSEK TETGGELECL 601 YRTEEGGRRI SRECRAEVOR ILHORAMDVK LDPALQDKCI IDLGKWGSEK TETGGELECL 602 YRTEEGGRRI SRECRAEVOR ILHORAMDVK LDPALQDKCI IDLGKWGSEK TETGGELECL 603 YRTEEGGRRI LADRALGDKCI IDLGKWGSEK TETGGELECL 701 QW7CHOVADN QIDSGDLWC LIQWKHOKDM NEKCAIGVTH FQLVQMKOFR FSYKFKWACK 701 QW7CHOVADN QIDSGDLWC LIQWKHOKDM NEKCAIGVTH FQLVQMKOFR FSYKFKWACK 701 QW7CHOVADN QIDSGDLWC LIQWKHOKDM NEKCAIGVTH FQLVQMKOFR FSYKFKWACK 801 CRCLRVZEL EWTEDIRLEP DLYEAGESDÍ KNFCSAVQYG NAQIIECLKE NKKQLSTRCH 801 CRCLRVZEL EWTEDIRLEP DLYEAGESDÍ KNFCSAVQYG NAQIIECLKE NKKQLSTRCH 801 LQCLKQNKNS ELMDPKCKQM ITKRQITQNT DYRLNPMLRK ACKADIEKFC HGILTKAKDD 901 LQCLKQNKNS ELMDPKCKQM ITKRQITQNT DYRLNPMLKSSKAD 901 LQCLKQNKNS ELMDPKCKQM ITKRQITQNT DYRLNPMLK ACKADIEKFC HGILTKAKDD 901 LQCLKQNKNS ELMDPKCKQM ITKRQITQNT DYRLNPMLK ACKADIEKFC HGILTKAKDD 901 LQCLKQNKNS ELMDPKCKQM ITKRQITQNT DYRLNPMLK ACKADIEKFC HGILTKAKDO 901 LQCLKQNKNS ELMDPKCKQM ITKRQITQNT DYRLNPMLKSSKAD 902 LQCLKQNKNS ELMDPKCKKOV INMLKSSKAD 903 LGCLKQNKNS ELMDPKCKQM INGKNS ELLKVNLLK IKTELCKKV INMLKSSKAD 904 LQCLKQNKNS ELMDPKCKOV INMLKSSKAD 905 LGCLKQNK
RAINEACESV IGTACKHIRS GDEMIESCLM EHLYTEKAVE DCEHRLLELO YRTEEGGRE, SRECRAEVOR ILHORAMDVK LDPALQDKCL IDLGKWCSEK QNFCHDVADN QIDSGDLMEC LIONKHOKDM NEKCAIGVTH FQLVQMKDFR QNFCHDVADN QIDSGDLMEC LIONKHOKDM NEKCAIGVTH FQLVQMKDFR QNFCHDVADN QIDSGDLMEC LIONKHOKDM NEKCAIGVTH FQLVQMKDFR CRRQLRVEEL EMTEDIRLEP DLYEACKSDI KNFCSAVQYG NAQIIECLKE CRRQLRVEEL EMTEDIRLEP DLYEACKSDI KNFCSAVQYG NAQIIECLKE LQCLKQNKNS ELMDPKCKOM ITKRQITQNT DYRLNPMLRK ACKADIPKFC LQCLKQNKNS ELMDPKCKOM ITKRQITQNT DYRLNPMLRK ACKADIPKFC LQCLKQNKNS ELMDPKCKOM ITKRQITQNT DYRLNPMLRK ACKADIPKFC LDQLQLHCS DEISSLCAEE AAAQEQTGQV EECLKVNLLK IKTELCKKEV LDPQLQLHCS DEISSLCAEE AAAQEQTGQV EECLKVNLLK IKTELCKKEV LDPQLQLHCS DEISSLCAEE AAAQEQTGQV EECLKVNLLK IKTELCKKEV RVALQPECKK RLNDRIEMMS YAAKVAPRADG FSDLAMQVMT SPSKNYILSV RVALQPECKK RLNDRIEMMS YAAKVAPRADG FSDLAMQVWT SPSKNYILSV	601 YRTEEGGRE, SRECRAEVOR ILHORAMDVK LOPALQDKCL IDLGKWGSEK 601 YRTEEGGRE, SRECRAEVOR ILHORAMDVK LOPALQDKCL IDLGKWGSEK 601 YRTEEGGRE, SRECRAEVOR ILHORAMDVK LOPALQDKCL IDLGKWGSEK 602 YRTEEGGRE, SRECRAEVOR ILHORAMDVK LOPALQDKCL IDLGKWGSEK 603 YRTEEGGRE, SRECRAEVOR ILHORAMDVK LOPALQDKCL IDLGKWGSEK 701 QNFCHDVADN QIDSGDLWEC LIONKHQKDM NEKCAIGVTH FQLVQWKDFR 801 CRRQLRVEEL EWTEDIRLEP DLYEACKSDI KNFCSAVQYG NAQIIECLKE 801 CRRQLRVEEL EWTEDIRLEP DLYEACKSDI KNFCSAVQYG NAQIIECLKE 801 LQCLKQNKNS ELMDPKCKQM ITKRQITQNT DYRLNPMLRK ACKADIPKFC 901 LDPQLQLHCS DEISSLCAEE AAAQEQTGQV EECLKVNLLK IKTELCKKEV 1001 LDPQLQLHCS DEISSLCAEE AAAQEQTGQV EECLKVNLLK IKTELCKKEV 1001 LDPQLQLHCS DEISSLCAEE AAAQEQTGQV EECLKVNLLK IKTELCKKEV 1101 RVALQPECKK RLNDRIEMWS YAAKVARPADG FSDLAMQVWT SPSKNYILSV 1101 RVALQPECKK RLNDRIEMWS YAAKVARPADG FSDLAMQVWT SPSKNYILSV
RALNEACESV IQTACKHIRS GDPMISSCLM RALNEACESV IQTACKHIRS GDPMISSCLM YRTEEQGRRI SRECRAEVQR ILHQRAMDVK OFFCHO-ADN GIDSGDLMEC LIQNKHQKDM OFFCHO-ADN GIDSGDLMEC LIQNKHQKDM OFFCHO-ADN GIDSGDLMEC LIQNKHQKDM CRRQLRVEEL EMTEDIRLEP DLYEACKSDI CRRQLRVEEL EMTEDIRLEP DLYEACKSDI CRRCLRVEEL EMTEDIRLEP DLYEACKSDI CRRCLRVEEL EMTEDIRLEP DLYEACKSDI CRRCLRONKNS ELMDPKCKQM ITKRQITQNT LQCLKQNKNS ELMDPKCKQM ITKRQITQNT LQCLKQNKNS ELMDPKCKQM ITKRQITQNT LDPQLQLHCS DEISSLCAEE AAAQEQTGQV LDPQLQLHCS DEISSLCAEE AAAQEQTGQV LDPQLQLHCS DEISSLCAEE AAAQEQTGQV RVALQPECKK RLNDRIEMWS YAAKVAPADG RVALQPECKK RLNDRIEMWS YAAKVAPADG RVALQPECKK RLNDRIEMWS YAAKVAPADG	601 YRTEEGGRE, SRECRAEVOR ILHGRAMDVK 601 YRTEEGGRRI SRECRAEVOR ILHGRAMDVK 601 YRTEEGGRRI SRECRAEVOR ILHGRAMDVK 602 YRTEEGGRRI SRECRAEVOR ILHGRAMDVK 601 YRTEEGGRRI SRECRAEVOR ILHGRAMDVK 701 QNFCHDVADN QIDSGDLMEC LIQNKHQKDM 701 QNFCHDVADN GIDSGDLMEC LIQNKHQKDM 701 QNFCHDVADN GIDSGDLMEC LIQNKHQKDM 701 QNFCHDVADN GIDSGDLMEC LIQNKHQKDM 801 CRRQLRVEEL EMTEDIALEP DLYEACKSDI 801 CRRQLRVEEL EMTEDIALEP DLYEACKSDI 801 LQCLKQNKNS ELMDPKCKQM ITKRQITQNT 901 LQCLKQNKNS ELMDPKCKQM ITKRQITQNT 901 LQCLKQNKNS ELMDPKCKQM ITKRQITQNT 1001 LDPQLQLHCS DEISSLCAEE AAAQEQTGQV 1001 LDPQLQLHCS DEISSLCAEE AAAQEQTGQV 1101 RVALQPECKK RLNDRIEMWS YAAKVAPPADG 1101 RVALQPECKK RLNDRIEMWS YAAKVAPPADG 1101 RVALQPECKK RLNDRIEMWS YAAKVAPPADG
RALNEACESV IQTACKHIRS RALNEACESV IQTACKHIRS YRTEEQGRRI SRECRAEVQR YRTEEQGRRI SRECRAEVQR YRTEEQGRRI SRECRAEVQR ONFCHOVADN QIDSGDLMEC QNFCHOVADN QIDSGDLMEC QNFCHOVADN QIDSGDLMEC CRRQLRVEEL EMTEDIRLEP LQCLKQNKNS ELMDPKCKQM LQCLKQNKNS ELMDPKCKQM LQCLKQNKNS ELMDPKCKQM LQCLKQNKNS ELMDPKCKQM LDPQLQLHCS DEISSLCAEE LDPQLQLHCS DEISSLCAEE LDPQLQLHCS DEISSLCAEE LDPQLQLHCS DEISSLCAEE RVALQPECKK RLNDRIEMWS RVALQPECKK RLNDRIEMWS	601 YRTEEQGRES SRECRAEVOR 601 YRTEEQGRES SRECRAEVOR 601 YRTEEQGRES SRECRAEVOR 602 YRTEEQGRES SRECRAEVOR 602 YRTEEQGRES SRECRAEVOR 701 QNFCHOVADN QIDSGDLMEC 801 CRRQLRVEEL EMTEDIRLEP 801 CRRQLRVEEL EMTEDIRLEP 801 LQCLKQNKNS ELMDPKCKQM 901 LQCLKQNKNS ELMDPKCKQM 1001 LDPQLQLHCS DEISSLCAEE 1001 LDPQLQLHCS DEISSLCAEE 1101 RVALQPECKK RLNDRIEMWS 1102 RVALQPECKK RLNDRIEMWS
RAINEACESV IQTACKHI RAINEACESV IQTACKHI YRTEEQGRRI SRECRAEV YRTEEQGRRI SRECRAEV YRTEEQGRRI SECRAEV YRTEEQGRRI SECRAEV OFFCHOVADN QIDSGDLM OFFCHOVADN QIDSGDLM OFFCHOVADN QIDSGDLM CRRQLRVEEL EMTEDIRL CRRQLRVEEL EMTEDIRL CRRQLRVEEL EMTEDIRL CRRQLRVEEL EMTEDIRL LQCLKQNKNS ELMDPKCK LQCLKQNKNS ELMDPKCK LQCLKQNKNS ELMDPKCK LQCLKQNKNS ELMDPKCK LDPQLQLHCS DEISSLCA LDPQLQLHCS DEISSLCA LDPQLQLHCS DEISSLCA LDPQLQLHCS DEISSLCA RVALQPECKK RLNDRIEM RVALQPECKK RLNDRIEM	601 YRTEEQGRRI 601 YRTEEQGRRI 601 YRTEEQGRRI 601 YRTEEQGRRI 701 QWFCHDVADN 701 QWFCHDVADN 701 QWFCHDVADN 701 QWFCHDVADN 701 QWFCHDVADN 801 CRRQLRVEEL 801 CRRQLRVEEL 801 CRRQLRVEEL 801 LQCLKQNKNS 901 LQCLKQNKNS 901 LQCLKQNKNS 1001 LDPQLQLHCS 1001 LDPQLQLHCS 1101 RVALQPECKK 1101 RVALQPECKK
	601 601 601 701 701 801 801 801 901 901 1001 1101
_ , ,	

19/23

Human antibody PAM-1 (clone 103/51)

Heavy chain sequence

CDR I

					•										•		
	TCC Ser									-							54
	CAC His 20															ATA Ile	108
	CI	R II					1						•				
· -	TAT Tyr		_						_				•		_		162
. – –	TCC											Met		Ser 70			216
	GAG Glu				_												270
			•	CI	RII	I		<u>.</u>			•	 	_				
-	TAC Tyr												-	313	2		

Fig. 17

20/23

Human antibody PAM-1 (clone 103/51)

Light chain sequence

GTG Val	ACC	TCC	TAT	GTG Val 5	CTG Leu	ACT	CAG Gln	CCA Pro	CCC Pro 10	Ser	GTG Val	TCA Ser	GTG Val	GCC Ala	Pro	GGA Gly	CAG Gln	54
ACG Thr	GCC Ala 20	ser	ATT	ACC Thr	TGT Cys	GGG Gly 25	GGA Gly	AAT Asn	AAC Asn	ATT	GGA Gly 30	AGT Ser	AAA Lys	AGT Ser	GTG Val	CAC His 35	TGG Trp	108
												•		(CDR :	ΙΙ		
TAC Tyr	CAT	CAG Gln	AAG Lys 40	CCA Pro	GGC Gly	CAG Gln	GCC Ala	CCT Pro 45	GTG Val	CTG Leu	GTC Val	GTC Val	TAT Tyr 50	GAT Asp	GAT Asp	AGC Ser	GAC Asp	162
CGG Arg 55	CCC Pro	TCA Ser	GGG	ATC Ile	CCT Pro 60	GAG Glu	CGA Arg	TTC Phe	TCT Ser	GGC Gly 65	TCC Ser	AAC Asn	TCT	GGG	AAC Asn 70	ACG Thr	GCC Ala	216
ACC Thr	CTG Leu	ACC Thr 75	ATC Ile	ACC Thr	AGG Arg	GTC Val	GAA Glu 80	GCC Ala	GGG Gly	GAT Asp	GAG Glu	GCC Ala 85	GAC Asp	TAT Tyr	TAC Tyr	TGT Cys	CAG Gln 90	270
				CD	RII	I								•			·	
GTG Val	TGG Trp	GAT Asp	AGT Ser	AGT Ser 95	AGT Ser	GAT Asp	CTC Leu	AAT Asn	TGG Trp 100	GTG Val	TTC Phe	GGC Gly	GGA Gly	AGG Arg 105	ACC Thr	CAA Gln	GCT Ala	324
GAC Asp	CGT Arg 110	CCT Pro	ACG Thr	TCA Ser	GCC Ala	CAA Gln 115	GGC Gly	TGC Cys	CCC Pro	TCC Ser	GGT Gly 120	CAC His	TCT Ser	GTT Val	CCC Pro	CGC Arg 125	CCC Pro	378
	CTG Leu			_			399											

Fig. 18

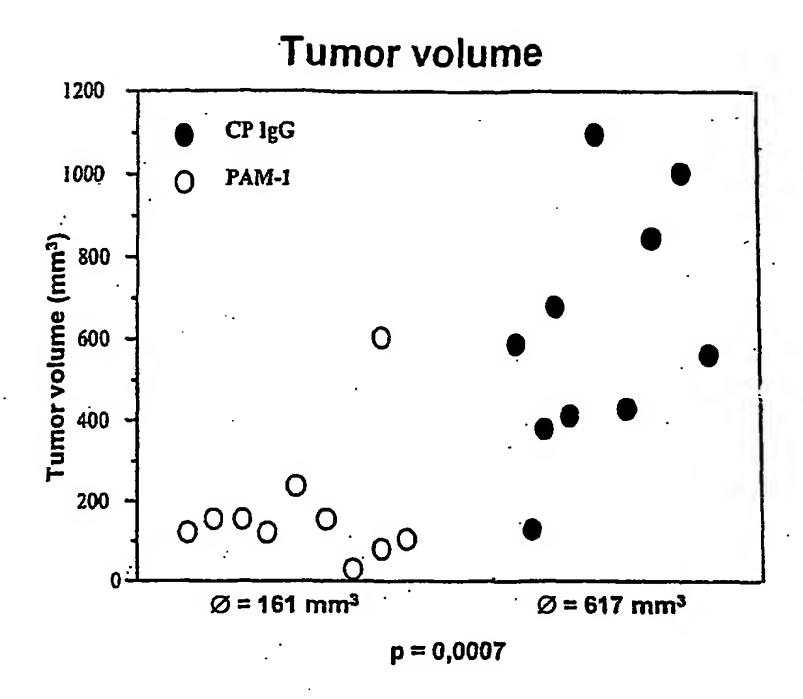


Fig. 19(A)

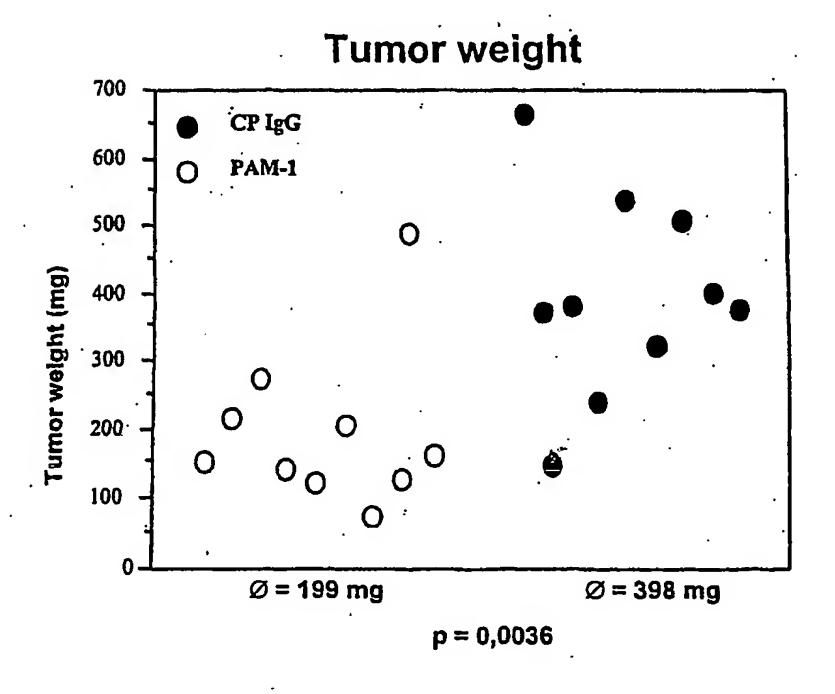


Fig. 19(B)

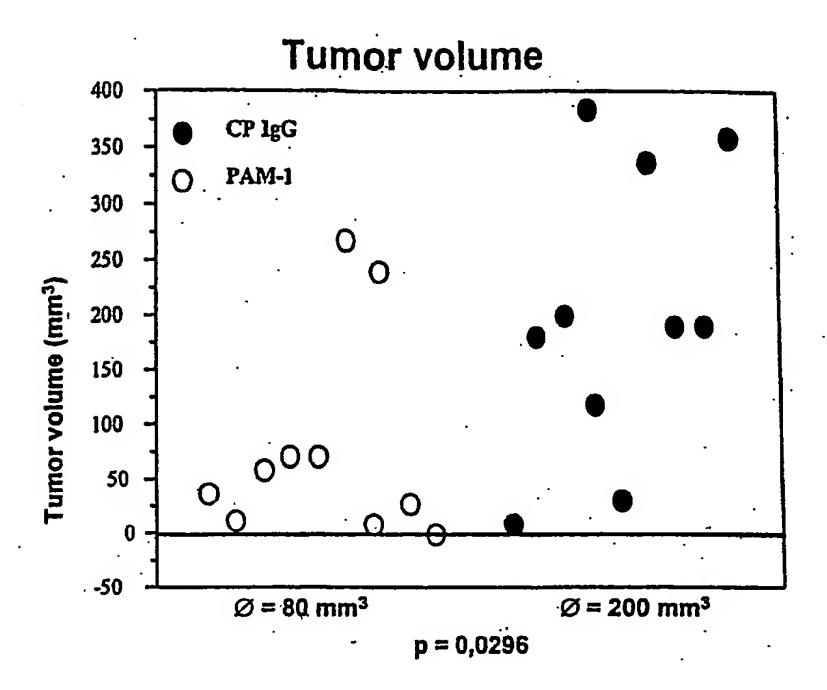


Fig. 20(A)

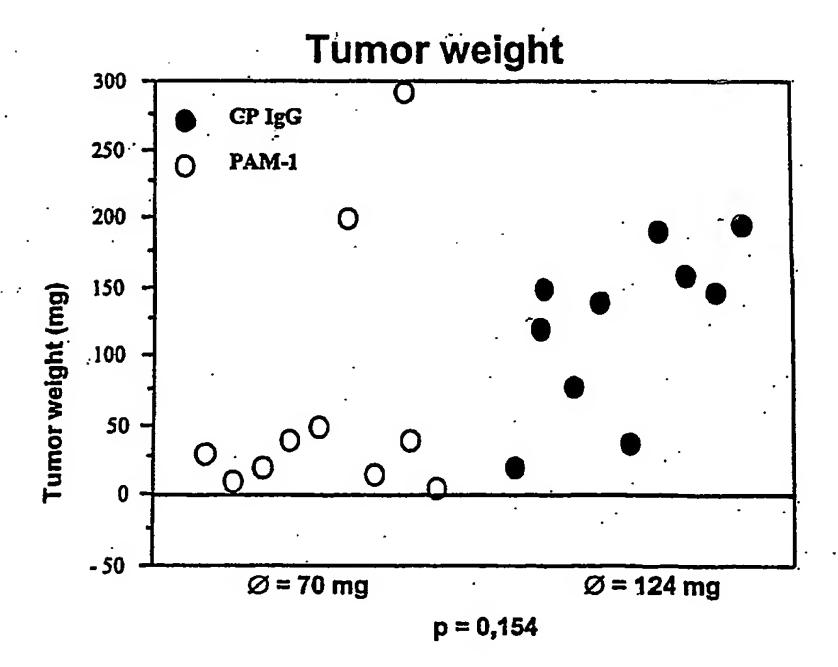
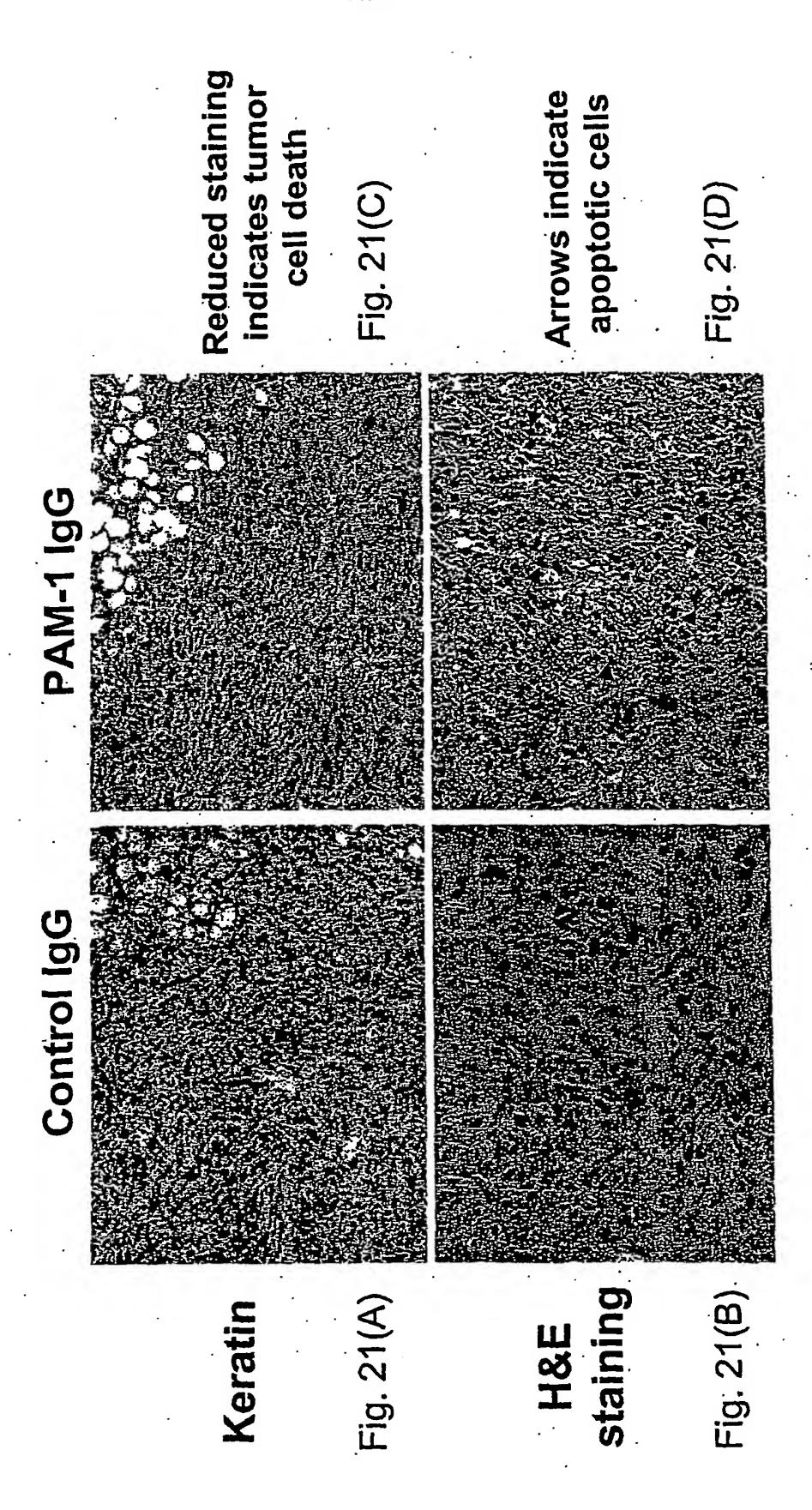


Fig. 20(B)



SUBSTITUTE SHEET (RULE 26)